



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 882

[Docket No. FDA-2022-N-3188]

Medical Devices; Neurological Devices; Classification of the Pediatric Autism Spectrum Disorder Diagnosis Aid

AGENCY: Food and Drug Administration, HHS.

ACTION: Final amendment; final order.

SUMMARY: The Food and Drug Administration (FDA, Agency, or we) is classifying the pediatric Autism Spectrum Disorder (ASD) diagnosis aid into class II (special controls). The special controls that apply to the device type are identified in this order and will be part of the codified language for the pediatric Autism Spectrum Disorder diagnosis aid's classification. We are taking this action because we have determined that classifying the device into class II (special controls) will provide a reasonable assurance of safety and effectiveness of the device. We believe this action will also enhance patients' access to beneficial innovative devices.

DATES: This order is effective [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. The classification was applicable on June 2, 2021.

FOR FURTHER INFORMATION CONTACT: Mohua Choudhury, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 4102, Silver Spring, MD 20993-0002, 240-402-3095, Mohua.Choudhury@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

Upon request, FDA has classified the pediatric Autism Spectrum Disorder diagnosis aid as class II (special controls), which we have determined will provide a reasonable assurance of safety and effectiveness. In addition, we believe this action will enhance patients' access to

beneficial innovation, in part by placing the device into a lower device class than the automatic class III assignment.

The automatic assignment of class III occurs by operation of law and without any action by FDA, regardless of the level of risk posed by the new device. Any device that was not in commercial distribution before May 28, 1976, is automatically classified as, and remains within, class III and requires premarket approval unless and until FDA takes an action to classify or reclassify the device (see 21 U.S.C. 360c(f)(1)). We refer to these devices as “postamendments devices” because they were not in commercial distribution prior to the date of enactment of the Medical Device Amendments of 1976, which amended the Federal Food, Drug, and Cosmetic Act (FD&C Act).

FDA may take a variety of actions in appropriate circumstances to classify or reclassify a device into class I or II. We may issue an order finding a new device to be substantially equivalent under section 513(i) of the FD&C Act (see 21 U.S.C. 360c(i)) to a predicate device that does not require premarket approval. We determine whether a new device is substantially equivalent to a predicate device by means of the procedures for premarket notification under section 510(k) of the FD&C Act (21 U.S.C. 360(k)) and part 807 (21 CFR part 807).

FDA may also classify a device through “De Novo” classification, a common name for the process authorized under section 513(f)(2) of the FD&C Act. Section 207 of the Food and Drug Administration Modernization Act of 1997 (Pub. L. 105-115) established the first procedure for De Novo classification. Section 607 of the Food and Drug Administration Safety and Innovation Act (Pub. L. 112-144) modified the De Novo application process by adding a second procedure. A device sponsor may utilize either procedure for De Novo classification.

Under the first procedure, the person submits a 510(k) for a device that has not previously been classified. After receiving an order from FDA classifying the device into class III under section 513(f)(1) of the FD&C Act, the person then requests a classification under section 513(f)(2).

Under the second procedure, rather than first submitting a 510(k) and then a request for classification, if the person determines that there is no legally marketed device upon which to base a determination of substantial equivalence, that person requests a classification under section 513(f)(2) of the FD&C Act.

Under either procedure for De Novo classification, FDA is required to classify the device by written order within 120 days. The classification will be according to the criteria under section 513(a)(1) of the FD&C Act. Although the device was automatically placed within class III, the De Novo classification is considered to be the initial classification of the device.

When FDA classifies a device into class I or II via the De Novo process, the device can serve as a predicate for future devices of that type, including for 510(k)s (see section 513(f)(2)(B)(i) of the FD&C Act). As a result, other device sponsors do not have to submit a De Novo request or premarket approval application to market a substantially equivalent device (see section 513(i) of the FD&C Act, defining “substantial equivalence”). Instead, sponsors can use the less-burdensome 510(k) process, when necessary, to market their device.

II. De Novo Classification

On November 3, 2020, FDA received Cognoa, Inc.’s request for De Novo classification of the Cognoa ASD Diagnosis Aid. FDA reviewed the request in order to classify the device under the criteria for classification set forth in section 513(a)(1) of the FD&C Act.

We classify devices into class II if general controls by themselves are insufficient to provide reasonable assurance of safety and effectiveness, but there is sufficient information to establish special controls that, in combination with the general controls, provide reasonable assurance of the safety and effectiveness of the device for its intended use (see 21 U.S.C. 360c(a)(1)(B)). After review of the information submitted in the request, we determined that the device can be classified into class II with the establishment of special controls. FDA has determined that these special controls, in addition to the general controls, will provide reasonable assurance of the safety and effectiveness of the device.

Therefore, on June 2, 2021, FDA issued an order to the requester classifying the device into class II. In this final order, FDA is codifying the classification of the device by adding 21 CFR 882.1491.¹ We have named the generic type of device pediatric Autism Spectrum Disorder diagnosis aid, and it is identified as a prescription device that is intended for use as an aid in the diagnosis of Autism Spectrum Disorder in pediatric patients.

FDA has identified the following risks to health associated specifically with this type of device and the measures required to mitigate these risks in table 1.

Table 1.--Pediatric Autism Spectrum Disorder Diagnosis Aid Risks and Mitigation Measures

Identified Risks	Mitigation Measures
Device failure or incorrect analysis leading to: <ul style="list-style-type: none">• False positives resulting in inappropriate patient treatment and potentially delayed diagnosis of a non-ASD condition• False negatives resulting in delayed diagnosis and patient treatment	Clinical performance testing; Software verification, validation, and hazard analysis; and Labeling
Use error or misinterpretation of results resulting in a false positive or false negative	Usability assessment, and Labeling

FDA has determined that special controls, in combination with the general controls, address these risks to health and provide reasonable assurance of safety and effectiveness. For a device to fall within this classification, and thus avoid automatic classification in class III, it would have to comply with the special controls named in this final order. The necessary special controls appear in the regulation codified by this order. This device is subject to premarket notification requirements under section 510(k) of the FD&C Act.

At the time of classification, pediatric Autism Spectrum Disorder diagnosis aids are for prescription use only. Prescription devices are exempt from the requirement for adequate directions for use for the layperson under section 502(f)(1) of the FD&C Act (21 U.S.C. 352(f)(1)) and 21 CFR 801.5, as long as the conditions of 21 CFR 801.109 are met.

¹ FDA notes that the “ACTION” caption for this final order is styled as “Final amendment; final order,” rather than “Final order.” Beginning in December 2019, this editorial change was made to indicate that the document “amends” the Code of Federal Regulations. The change was made in accordance with the Office of Federal Register’s (OFR) interpretations of the Federal Register Act (44 U.S.C. chapter 15), its implementing regulations (1 CFR 5.9 and parts 21 and 22), and the Document Drafting Handbook.

III. Analysis of Environmental Impact

The Agency has determined under 21 CFR 25.34(b) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

IV. Paperwork Reduction Act of 1995

This final order establishes special controls that refer to previously approved collections of information found in other FDA regulations and guidance. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3521). The collections of information in 21 CFR part 860, subpart D, regarding De Novo classification have been approved under OMB control number 0910-0844; the collections of information in 21 CFR part 814, subparts A through E, regarding premarket approval, have been approved under OMB control number 0910-0231; the collections of information in part 807, subpart E, regarding premarket notification submissions, have been approved under OMB control number 0910-0120; the collections of information in 21 CFR part 820, regarding quality system regulation, have been approved under OMB control number 0910-0073; and the collections of information in 21 CFR parts 801, regarding labeling, have been approved under OMB control number 0910-0485.

List of Subjects in 21 CFR Part 882

Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 882 is amended as follows:

PART 882--NEUROLOGICAL DEVICES

1. The authority citation for part 882 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 360l, 371.

2. Add § 882.1491 to subpart B to read as follows:

§ 882.1491 Pediatric Autism Spectrum Disorder diagnosis aid.

(a) *Identification.* A pediatric Autism Spectrum Disorder diagnosis aid is a prescription device that is intended for use as an aid in the diagnosis of Autism Spectrum Disorder in pediatric patients.

(b) *Classification.* Class II (special controls). The special controls for this device are:

(1) Clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use, including an evaluation of sensitivity, specificity, positive predictive value, and negative predictive value using a reference method of diagnosis and assessment of patient behavioral symptomology.

(2) Software verification, validation, and hazard analysis must be provided. Software documentation must include a detailed, technical description of the algorithm(s) used to generate device output(s), and a cybersecurity assessment of the impact of threats and vulnerabilities on device functionality and user(s).

(3) Usability assessment must demonstrate that the intended user(s) can safely and correctly use the device.

(4) Labeling must include:

(i) Instructions for use, including a detailed description of the device, compatibility information, and information to facilitate clinical interpretation of all device outputs; and

(ii) A summary of any clinical testing conducted to demonstrate how the device functions as an interpretation of patient behavioral symptomology associated with Autism Spectrum Disorder. The summary must include the following:

(A) A description of each device output and clinical interpretation;

(B) Any performance measures, including sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV);

(C) A description of how the cutoff values used for categorical classification of diagnoses were determined; and

(D) Any expected or observed adverse events and complications.

(iii) A statement that the device is not intended for use as a stand-alone diagnostic.

Dated: December 27, 2022.

Lauren K. Roth,

Associate Commissioner for Policy.

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